

Hormone curbs depressive-like symptoms in stressed mice

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A hormone with anti-diabetic properties also reduces depression-like symptoms in mice, researchers from the School of Medicine at the UT Health Science Center San Antonio reported today.

All types of current antidepressants, including tricyclics and [selective serotonin reuptake inhibitors](#), increase the risk for [type 2 diabetes](#). "The finding offers a novel target for [treating depression](#), and would be especially beneficial for those [depressed individuals](#) who have type 2 diabetes or who are at high risk for developing it," said the study's senior author, Xin-Yun Lu, Ph.D., associate professor of pharmacology and psychiatry and member of the Barshop Institute for Longevity and Aging Studies at the UT Health Science Center.

The hormone, called adiponectin, is secreted by adipose tissue and sensitizes the body to the action of insulin, a hormone that lowers blood sugar. "We showed that adiponectin levels in plasma are reduced in a chronic social defeat stress model of depression, which correlates with the degree of social aversion," Dr. Lu said.

Facing Goliath over and over

In the study mice were exposed to 14 days of repeated social defeat stress. Each male mouse was introduced to the home cage of an unfamiliar, aggressive resident mouse for 10 minutes and physically defeated. After the defeat, the resident mouse and the intruder mouse

each were housed in half of the cage separated by a perforated plastic divider to allow visual, olfactory and auditory contact for the remainder of the 24-hour period. Mice were exposed to a new resident mouse cage and subjected to social defeat each day. Plasma adiponectin concentrations were determined after the last social defeat session. Defeated mice displayed lower plasma adiponectin levels.

Withdrawal, lost pleasure and helplessness

When adiponectin concentrations were reduced by deleting one allele of the adiponectin gene or by a neutralizing antibody, mice were more susceptible to stress-induced [social withdrawal](#), anhedonia (lost capacity to experience pleasure) and learned helplessness.

Mice that were fed a high-fat diet (60 percent calories from fat) for 16 weeks developed obesity and type 2 diabetes. Administration of adiponectin to these mice and [mice](#) of normal weight produced antidepressant-like effects.

Possible innovative approach for depression

"These findings suggest a critical role of adiponectin in the development of depressive-like behaviors and may lead to an innovative therapeutic approach to fight depression," Dr. Lu said.

A novel approach would benefit thousands. "So far, only about half of the patients suffering from major depressive disorders are treated to the point of remission with antidepressant drugs," Dr. Lu said. "The prevalence of depression in the diabetic population is two to three times higher than in the non-diabetic population. Unfortunately, the use of current antidepressants can worsen the control of diabetic patients. Adiponectin, with its anti-diabetic activity, would serve as an innovative

therapeutic target for depression treatments, especially for those individuals with diabetes or prediabetes and perhaps those who fail to respond to currently available antidepressants."

The study is published in this week's *Proceedings of the National Academy of Sciences*.

More information: "Adiponectin is critical in determining susceptibility to depressive behaviors and has antidepressant-like activity," by Jing Liu et al. *PNAS*.

Provided by University of Texas Health Science Center at San Antonio

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